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EXAMINER	
KIM, ALEXANDER D	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,064	DEMMER ET AL.	
	Examiner	Art Unit	
	ALEXANDER D. KIM	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-16* is/are pending in the application.

4a) Of the above claim(s) *16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/21/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Sartobind® Membrane Adsorbers brochure-A (2003), Fischer-Fruhholz, May 16, 2003, Applications Membrane Adsorbers, Sartobind® Membrane Adsorbers brochure by Hirai et al., 29, Sept 2003, Virus Purification and Removal with Sartobind® Membrane Adsorbers.

DETAILED ACTION

Application Status

1. By virtue of a preliminary amendment filed on 01/25/2008, claims 1 and 3-16 have been amended; claim 2 has been canceled. Thus, claims 1 and 3-16 are pending in this instant case.

Election

2. Applicant's election with traverse of Group I (Claims 1, 3-15) in a paper filed on 01/25/2008 is acknowledged. The traversal is on the ground(s) that all the claims share a unity of invention because of the amended claim 1 recites the limitation "a molecular weight greater than 1x 10^6 Da", wherein the Castilho et al. only describe high-molecular compound having molecular weight of only 900,000 Da at most (although, Applicants recited "900,0000" in the Remarks filed on 1/25/2008, the large IgM has about 900 kDa). This is not found persuasive because this feature is taught by the prior art by Sartobind® Membrane Adsorbers brochure by Hirai et al. (29, Sept 2003, Virus Purification and Removal with Sartobind® Membrane Adsorbers), who teaches the method of purifying the PrV virus, which has a molecular weight of at least 90x10^6 to 95x10^{6}" as evidenced by Stevely (Journal of Virology, 1977, volume 22, pages 232-234). The new reference was necessitated by the instant claim amendment. Thus, the amended technical feature is not special because it does not constitute an advance over the prior art by Sartobind© Membrane Adsorbers brochure by Hirai et al. as

evidenced by Stevely (Journal of Virology, 1977, volume 22, pages 232-234). The requirement is still deemed proper and is therefore made FINAL.

Claim 16 is withdrawn from further consideration as non-elected inventions. Claims 1 and 3-15 will be examined herein.

Priority

3. The instant application is a 371 filing of the International Application No. PCT/EP05/00810 filed on 01/27/2005. The Examiner notes that the requirements of national stage entry of the instant application had been completed (note assigned U.S. filing date) within 30 months of the earliest claimed priority date; the related international application includes both a search report and a preliminary examination report.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to a foreign patent application 10 2004 004 043.5 (Germany) filed without English translation on 1/27/2004.

Information Disclosure Statement

4. The information disclosure statement (IDS) filed on 07/21/2006 has been reviewed, and its references have been considered as shown by the Examiner's initial on the attached copy.

Objections to the Specification

5. The specification is objected to because of the following informalities:

(a) The specification is objected to because the title is not descriptive of the claims. A new title is required that is clearly indicative of the invention to which the claims are drawn (see M.P.E.P. § 606.01). The examiner suggests the following new title, for example: ---A method of purification of high-molecular compounds by means of affinity membrane chromatography---

(b) The Abstract is missing. The copy of the cover page from the PCT publication were used for Abstract. However, it only recites "see Original for English" in the place of Abstract. Appropriate correction is required.

Claim Objections

6. Claims 1, 3-15 are objected to because of the following informalities:

(a) Claim 1 is objected because the use of abbreviation "Da". It should be spelled out on a first appearance in claims. Appropriate correction is required.

(b) Claim 13 is objected because the use of abbreviation "DEAE, DEA, CM, QA, TMA, S, SP". It should be spelled out on a first appearance in claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1 and 3-15 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to a method for purifying and/or isolating high-molecular compounds contained in a solution or a suspension with the capacity for metal chelate formation, the method comprising the steps of: (a) applying a solution or suspension containing high-molecular compounds onto a metal ions containing membrane; and (b) separating the high-molecular compounds by affinity chromatography by binding them to the metal ions containing membrane, wherein the high-molecular compounds have a molecular weight greater than $1x10^6$ Da. Claims 3-15 are drawn to the method of Claim 1 with additional limitations as recited in claims.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure

of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (paraphrased from *Enzo Biochemical Inc. v. Gen-Probe Inc.* (CAFC (2002) 63 USPQ2d 1609).

University of Rochester v. G.D. Searle & Co. (69 USPQ2d 1886 (2004)) specifically points to the applicability of both *Lily* and *Enzo Biochemical* to methods of using products, wherein said products lack adequate written description. While in *University of Rochester v. G.D. Searle & Co.* the methods were held to lack written description because not a single example of the product used in the claimed methods was described, the same analysis applies wherein the product, used in the claimed methods, must have adequate written description as noted from *Enzo Biochemical* (see above).

The instant specification teach a method for purifying and/or isolating high-molecular compounds contained in a solution or a suspension with the capacity for metal chelate formation, the method comprising the steps of: (a) applying a solution or suspension containing the high-molecular compounds bacteriophage M13 onto the Sartobind® Membrane with imidodiacetic acid (IDA) type 19442 with Cu2+ ions; and (b) separating the bacteriophage M13 by Sartobind® Membrane (with imidodiacetic acid attached as binding entity or functional group). The breadth of claim includes a method step involving a solution of any high molecular weight compound (including but

not limited to any proteins, any protein like compounds, any biopolymers, any lipids, any micells and any liposomes) as long as it has molecular weight of greater than $1x10^6$ Da; and/or involving any affinity chomatography having any membrane (containing a metal ions) made up of any materials. The prior art by the prior art by Sartobind® Membrane Adsorbers brochure by Hirai et al. (29, Sept 2003, Virus Purification and Removal with Sartobind® Membrane Adsorbers) teaches the method of purifying the PrV virus, which has a molecular weight of at least $90x10^6$ to $95x10^6$ as evidenced by Stevely (Journal of Virology, 1977, volume 22, pages 232-234), which is encompassed by the breadth of Claims 1 and 3-15. The specification discloses one method described above using Sartobind® Membrane with imidodiacetic acid (IDA) type 19442, which is encompassed by the breadth of Claims 1 and 3-15. However, the prior art and the instant specification do not describe the claimed genus method as disclosed in the breadth of claims above comprising purification of any high molecular compound, and/or steps involving any metal ion affinity chromatography with any membrane (containing metal ions) made up of any material. Also, the claimed method in Claim 1 is not limited to the use of particular affinity chromatography (that is the affinity are created by the metal chelating property of membrane and the high molecular compounds) as long as the membrane used in chromatography contains a metal (e.g., metal ions from a buffer). A method of instant specification and prior arts do not describe a genus method, as described in the breadth of claims, sufficiently to represent the correlation between the structure of any high molecular compound, any affinity membrane used in steps and function of purifying any high molecular compound having molecular weight greater than $1x10^6$ Da. Thus

the instant specification and the prior art cannot describe the structure of a very broad claimed genus and one skilled in the art would not be in possession of the claimed genus by the instant specification.

8. Claims 1 and 3-15 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for method comprising the steps of applying a solution or suspension containing the high-molecular compounds bacteriophage M13 onto the Sartobind® Membrane Adsobers with an imidodiacetic acid (IDA) type 19442 charged with Cu^{2+} ions and separating the bacteriophage M13; does not reasonably provide enablement for a method step involving a solution of any high molecular weight compound (including but not limited to any proteins, any protein like compounds, any biopolymers, any lipids, any micells and any liposomes) as long as it has molecular weight of greater than $1x10^6$ Da; and/or involving any affinity chomatography having any membrane (in the presence of a metal ions) made up of any materials.

The specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use of the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to

practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The nature of the invention is drawn to a method for purifying and/or isolating high-molecular compounds contained in a solution or a suspension with the capacity for metal chelate formation, the method comprising the steps of: (a) applying a solution or suspension containing the high-molecular compounds bacteriophage M13 onto the Sartobind® Membrane with imidodiacetic acid (IDA) type 19442 charged with Cu^{2+} ions; and (b) separating the bacteriophage M13. The breadth of claim includes a method step involving a solution of any high molecular weight compound (including but not limited to any proteins, any protein like compounds, any biopolymers, any lipids, any micells and any liposomes) as long as it has molecular weight of greater than $1x10^6$ Da; and/or involving an affinity chomatography by any membrane (containing a metal ions)

made up of any materials. Applicants teach a method of purifying M13 bacteriophage using a commercially available Sartobind® Membrane with imidodiacetic acid (IDA) type 19442 with Cu^{2+} ions. Also, the prior art by the prior art by Sartobind® Membrane Adsorbers brochure by Hirai et al. (29, Sept 2003, Virus Purification and Removal with Sartobind® Membrane Adsorbers) teaches the method of purifying the PrV virus, which has a molecular weight of at least $90x10^6$ to $95x10^6$ as evidenced by Stevely (Journal of Virology, 1977, volume 22, pages 232-234). However, applicants and prior arts disclose no direction or guidance on how to make and use any other representative species for claimed genus method, that is a method comprising step of using any affinity chromatography having any membrane containing a metal ions for purifying any high molecular weight (MW) compound as long as the molecular weight is greater than $1x10^6$ Da. Thus, the specification and prior art fail to describe how to make and use the claimed genus method sufficiently. Therefore, it is unpredictable for claimed genus method to be used in the method of purifying any high molecular weight compound (i.e., MW of more than $1x10^6$ Da). Thus, it is unpredictable for any high-molecular compound purification method encompassed by the breadth of claims for one skilled in the art to make and use the full scope of claims. The said unpredictability makes the relative skill required in the art very high. For all of the above reason, it would require undue experimentation necessary for the claimed method for purifying any high-molecular compounds.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1 and 3-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sartobind® Membrane Adsorbers brochure-A (2003, see the attachment) as evidenced by Fischer-Fruhholz (May 16, 2003, Applications Membrane Adsorbers, see the attachemnt) and Stevely (Journal of Virology, 1977, volume 22, pages 232-234), and in view of Sartobind® Membrane Adsorbers brochure by Hirai et al. (29, Sept 2003, Virus Purification and Removal with Sartobind® Membrane Adsorbers, see the attachment).

Claim 1 is drawn to a method for purifying and/or isolating high-molecular compounds contained in a solution or a suspension with the capacity for metal chelate formation, the method comprising the steps of: (a) applying a solution or suspension containing high-molecular compounds onto a metal ions containing membrane; and (b) separating the high-molecular compounds by affinity chromatography by binding them to the metal ions containing membrane, wherein the high-molecular compounds have a molecular weight greater than $1x10^6$ Da. Claims 3-15 are drawn to the method of Claim 1 with additional limitations as recited in claims.

Sartobind® Membrane Adsorbers brochure-A teach a method of purification using "Sartobind MultiSep Membrane Adsorbers" which is used in chromatography as

shown in the figures on page 5, wherein the membrane type includes "Sartobind IDA (iminodiacetic acid) metal chelate", wherein the applications includes "Viral purification" (see middle, under the Application on page 6). Thus, Sartobind® Membrane Adsorbers brochure teach a step of applying a solution containing high molecular biopolymers as exemplified by the graph showing the UV detection vs. flow rate of a column chromatography (see page 2) and separating virus as indicated under "Applications" (see page 6, middle); and meets the limitation of claim 1, 3 and 8 except molecular weight of $1x10^6$. The Sartobind® Membrane Adsorbers is made of "cellulose" (see top of page 1) and have pore size of "3-5 um" (see top of page 4), which meets the limitation of claims 6-7.

Sartobind® Membrane Adsorbers with Cu^{2+} is evidenced by the teaching of charging with Cu^{2+} as evidenced by Fischer-Fruhholz (see page 5); thus, meeting the limitation of claims 4-5.

Sartobind® Membrane Adsorbers brochure by Hirai et al. teach that the Sartobind® Membrane Adsorbers is used to purify a virus including "pseudorabies virus (PrV)" on page 32, wherein the PrV has molecular weight greater than $1x10^6$ because "The whole native DNA has a molecular weight of $90x10^6$ to $95x10^6$" (see Abstract of Stevely).

Sartobind® Membrane Adsorbers brochure-A does not teach a method for purifying virus (i.e., a high-molecular compounds) with a molecular weight greater than $1x10^6$ Da and a method step of additional ion exchange chromatography prior to step (a) of Claim 1, or additional filtration for the removal of additional impurities.

Comment [RH1]: Why wouldn't this be a 102???

Comment [AK2]: I thought about it but the Sartobind® Membrane Adsorbers brochure by Hirai et al. teach cation exahnge which could have trace of metal ions in the buffer but the buffer used before the loading the virus does not have metal ions and the Claim 1 recites loading "to the metal ions containing membrane". The ref teach having K metal ion in the elution buffer and I think this is different from the limitation.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply a solution containing PrV virus particle to the membrane type includes Sartobind IDA (iminodiacetic acid) Cu^{2+} metal chelate for viral purification, because the PrV was tested in the Sartobind® Membrane Adsorbers with different binding functional groups (see Test condition, middle of Sartobind® Membrane Adsorbers brochure by Hirai et al.) with reasonable expectation of success. It would have been also obvious to one of ordinary skill in the art at the time the invention was made to apply a solution containing PrV virus an additional ion exchange or filtration as taught by Sartobind® Membrane Adsorbers brochure by Hirai et al. (see method of using Sartobind S100 cation exchanger, in the middle of left column) because additional purification step results in more pure product after purification.

One would have been motivated to do so because Sartorius teach the "application of Sartobind Membrane Adsorbers is advantageous especially in purification and removal of viruses for biopharmaceutical process" (see Sartobind® Membrane Adsorbers brochure by Hirai et al., Summary at the end). All physical characteristics of the Sartobind Membrane Adsorbers are already described above, which meets the limitation of Claims 9-12. Fischer-Fruhholz also disclose the Sartobind® Membrane Adsorbers is used for "Clearance of endotoxin" (see page 23), which meets the limitation of method in claim 14. Thus, the invention taken as a whole is *prima facie* obvious.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEXANDER D. KIM whose telephone number is (571)272-5266. The examiner can normally be reached on 11AM-7:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alexander D Kim/
Examiner, Art Unit 1656

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652